REMARKS

Applicants request favorable reconsideration and allowance of the subject application in view of the following remarks.

Claims 1-17 remain pending in the application, with claims 1, 8 and 9 being independent.

Applicant requests favorable reconsideration and withdrawal of the rejections set forth in the above-noted Office Action.

The rejection of claims 1-17 technically under 35 U.S.C. §112, first paragraph, as lacking enablement, is respectfully traversed. The Examiner has noted that the subject specification reasonably demonstrates a composition consisting essentially of chlorogenic acid and 3-o-p-Coumaryl quinic acid, however, the Examiner further notes that no working examples or data thereof are provided for a pharmaceutical composition consisting essentially of chlorogenic acid and p-Coumaryl quinic acid. Applicants wish to point out that, Applicants' invention relates to a pharmaceutically effective amount of chlorogenic acid and 3-o-p-Coumaryl quinic acid isolated from any plant parts of *Piper betel* or any other source, optionally along with pharmaceutically acceptable additives, therefore, under the Examiners own admission, Applicants' invention is enabled under 35 U.S.C. §112, first paragraph. As such, reconsideration and withdrawal of the § 112 rejection is respectfully requested.

Claims 1-17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kuroda et al. (Mutation Research/Reviews in Mutation Research, Volume 436, Issue 1, January 1999, Pages 69-97) in view of Yang et al. (Drug Metabolism Reviews, Volume 33, Issues 3 & 4, December 2001, Pages 237-253). Claims 1-17 were also rejected under 35 U.S.C. § 103(a) as

being unpatentable over Ferguson (Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis, Volume 475, Issues 1 & 2, April 18, 2001, Pages 89-111). Claims 1-17 were also rejected under 35 U.S.C. § 103(a) as being unpatentable over Yang et al. (Drug Metabolism Reviews, Volume 33, Issues 3& 4, December 2001, Pages 237-253). Applicants submit that the cited art, whether taken individually or in combination, does not teach or suggest many features of the present invention, as previously recited in these claims. Therefore, these rejections are respectfully traversed.

In one aspect of the present invention, independent claim 1 recites a method of treating acute and chronic myeloid leukemia (AML & CML) and lymphoid leukemia, in a mammal, in order to obtain a percentage growth inhibition of at least one of promonocyte cells, Erythroleukemia cells, or CML's leukemic cells. The method comprises administering a pharmaceutical composition that is a synergistic combination consisting essentially of a pharmaceutically effective amount of chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ) isolated from any plant parts of *Piper betel* or any other source, optionally along with pharmaceutically acceptable additives.

In another aspect of the present invention, independent claim 8 recites a method, of treating AML & CML and lymphoid leukemia, in a mammal, in order to obtain a percentage growth inhibition of at least one of promonocyte cells, Erythroleukemia cells, or CML's leukemic cells. The method comprises administering a pharmaceutical composition, consisting essentially of a pharamaceutically effective amount of CA isolated from any plant parts of *Piper*

betel or any other source, optionally along with pharmaceutically acceptable additives wherein the percentage growth inhibition of Erythroleukemia cells is up to about 30% with CA.

In a further aspect of the present invention, independent claim 9 recites a method of treating AML & CML and lymphoid leukemia, in a mammal, in order to obtain a percentage growth inhibition of at least one of promonocyte cells, Erythroleukemia cells, or CML's leukemic cells. The method comprises administering a pharmaceutical composition, consisting essentially of a pharamaceutically effective amount of PCQ isolated from any plant parts of *Piper betel* or any other source, optionally along with pharmaceutically acceptable additives, wherein the percentage growth inhibition of Erythroleukemia cells is up to about 8% with PCQ.

Applicants submit that the cited art, whether taken individually or in combination, does not teach or suggest such features of Applicants' present invention, as recited in independent claims 1, 8 and 9.

The Examiner considers Kuroda et al. to teach an antimutagenic activity against various mutagens of tea extracts of green and black teas and polyphenols including ECG and EGCG, demonstrated in microbial systems *Salmonella typhimurium* and *Escherichia coli*, mammalian cell systems and *in vivo* animal tests. The Examiner further considers Kuroda et al. to teach that the anticarcinogenic activity of tea phenols has been shown in experimental animals such as rats and mice, in leukemia. The Examiner notes, however, that Kuroda et al. fails to teach the polyphenols of the black and green teas, CA and PCQ, mode of administration, dose levels administered, and percentage growth inhibition as recited in independent claims 1, 8, and 9. It is the Examiners position, however, that Yang et al. meets the deficiencies of Kuroda et al., by

teaching the polyphenols of black and green teas as inclusive of CA and quinic acid, which is useful in prevention of carcinogenesis, therefore rendering Applicants' invention obvious.

Applicants submit however, that Yang et al. fails to overcome the deficiencies of Kuroda et al. Yang et al. relates to the status of tea as a possible cancer chemopreventive agent. In addition, any mention to polyphenols of tea by Yang et al. refers to chlorogenic acid (CA) and 4-coumarylquinic acid and not 3-o-p Coumaryl quinic acid (PCQ). Applicants submit, therefore, that it is at least the inclusion of chlorogenic acid (CA) and 3-o-p Coumaryl quinic acid (PCQ) which is necessary to render Applicants' invention obvious. Applicants submit, therefore, that Yang et al. fails to overcome the many deficiencies of Kuroda et al. In addition to the PCQ, as noted by the Examiner, Yang et al. also fails to teach or disclose treating acute and chronic leukemia and lymphoid leukemia, the additives, the amount ratio of CA and PCQ, the mode of administration, dose levels administered, and the percentage growth inhibition as recited in independent claims 1, 8, and 9 of Applicants' invention.

The Examiner also considers the Ferguson publication to teach a green tea extract that comprises polyphenols such as epigallocatechin gallate, chlorogenic acid and coumarylquinic acid. The Examiner notes however, that Ferguson fails to teach the method of treating acute and chronic leukemia and lymphoid leukemia, the additives, the amount of CA and PCQ, the mode of administration, does levels administered, or the percentage growth inhibition claimed. Applicants wish to add that in addition to the numerous deficiencies of Ferguson noted by the Examiner, Ferguson merely discloses coumarylquinic acid and not 3-o-p Coumaryl quinic acid. Applicants submit, therefore, that Ferguson and Yang et al. add nothing to the teachings of the

Kuroda et al. document that would render obvious Applicants' present invention, as recited in the independent claims.

Applicants further submit that it would not have been obvious to one skilled in the art to use either 4-coumarylquinic acid or coumaryl quinic acid as disclosed in Yang et al. and Ferguson respectively, instead of 3-o-p Coumaryl quinic acid, for the treatment of acute and chronic myeloid leukemia and lymphoid leukemia in mammals. As noted in Applicants' specification, it is the presence of the hydroxyl group at C-3 position of the aromatic ring, which gives stronger activity to CA in destroying both CD33- and CD33+ cells and also lymphoid leukemic cells. In addition, the Examiner notes on pages 4 & 5 of the above referenced Office Action that

> [i]t is also known that p-coumaryl quinic acid exists as 3-o-p-coumarylquinic acid, 4-o-p-coumarylquinic acid, and 5-o-p-coumarylquinic acid, for example. Thus, given such differences in the molecular structure of such p-coumaryl quinic acids and in the absence of a showing that the structural disparity between any and all p-coumaryl quinic acid exhibits the same functional effect for inhibition of growth leukemic acid cell lines of cell type K562 in either an *in vitro* or *in vivo test* model, it is not reasonable to predict that a claim-designation composition comprising any and all p-coumaryl quinic acids would provide the same beneficial functional effect for the treatment of acute and chronic myeloid leukemia in animals and humans.

Applicants submit, therefore, that it would not have been obvious to one skilled in the art to use either 4-coumarylquinic acid or coumaryl quinic acid for the treatment of acute and chronic myeloid leukemia and lymphoid leukemia in mammals.

For the foregoing reasons, Applicant submits that the present invention, as recited in

independent claims 1, 8 and 9, is patentably defined over the cited art, whether that art is taken individually or in combination.

Dependent claims 2-7 and 10-17 also should be deemed allowable, in their own right, for defining other patentable features of the present invention in addition to those recited in their respective independent claims. Further individual consideration of these dependent claims is requested.

Applicant submits that the instant application is in condition for allowance. Applicant, therefore, also requests favorable reconsideration, withdrawal of the rejection set forth in the above-noted Office Action, and an early notice of allowance.

Any additional fee required to render this response timely may be charged to Deposit Acct. No. 06-1205. All correspondence should continue to be directed to the below-listed address.

The undersigned attorney of record may be reached in Washington, DC by telephone at (202) 530-1010.

Respectfully submitted,

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